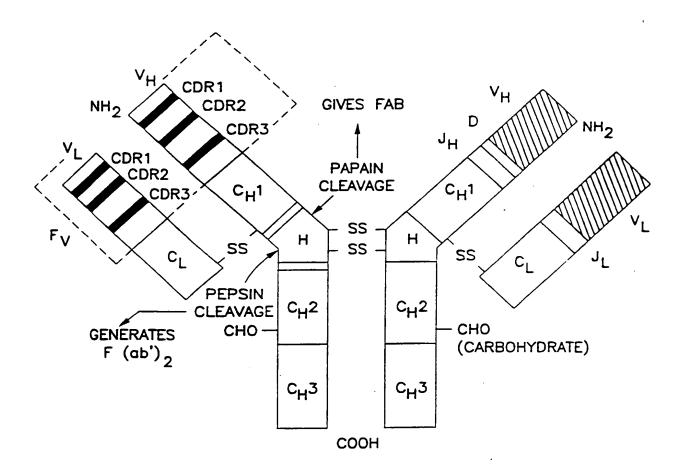
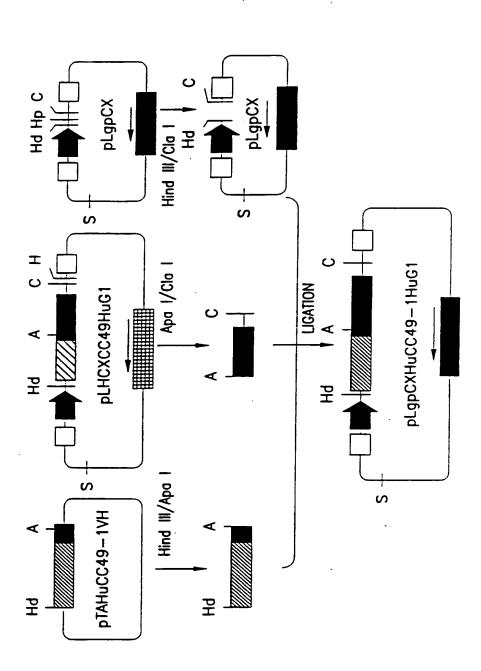
FIG. 1



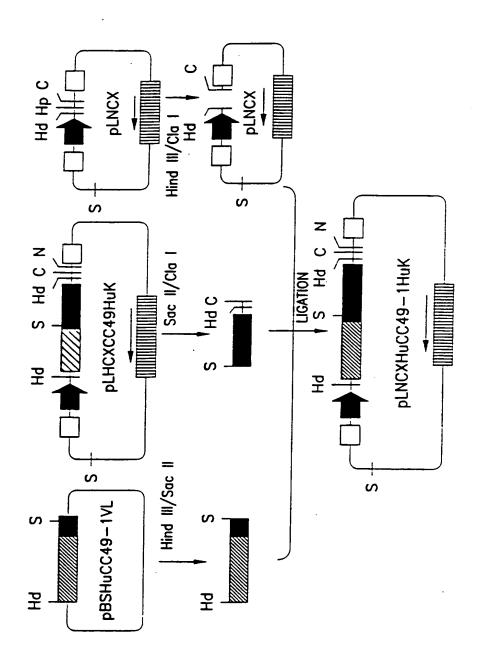
CDR 1							
24         25         26         27         a         b         c         d         e         d         e         d         e         d         e         d         e         d         e         d         e         d         e         d         e         d         e         d         e         d         e         d         e         d         e         d         e         d         e         e         d         e         e         e         e         e         e         e         e         e         e         e         e         e         e         e         e         e         e         e         e         e         e         e         e         e         e         e         e         e         e         e         e         e         e         e         e         e         e         e         e         e         e         e         e         e         e         e         e         e         e         e         e         e         e         e         e         e         e         e         e         e         e         e         e         e         e <td>34 Ala Ala</td> <td></td> <td></td> <td></td> <td></td> <td>65 Gly Gly</td> <td></td>	34 Ala Ala					65 Gly Gly	
24         25         26         27         o         b         c         d         e         f         28         29         30         31           Lys         Ser         Gln         Ser         Val         Leu         Tyr         Ser         Gln         Ser         Val         Leu         Tyr         Ser         Asn         Gln         Ser         Lys         Asn         Gln         Ser         Tyr         Asn         Glu         Ser         Tyr         Tyr         Asn         Glu         Ser         Tyr         Tyr         Ser         Tyr         Tyr         Ser         Tyr	33 Feu Feu					64 Lys Gln	
24         25         26         27         a         b         c         d         e         f         28         29         30           Lys         Ser         Ser         Gin         Ser         In         Ser         In         In </td <td>32 Tyr Tyr</td> <td></td> <td></td> <td></td> <td></td> <td>63 Phe Phe</td> <td></td>	32 Tyr Tyr					63 Phe Phe	
24         25         26         27         0         b         c         d         e         f1         28         G1         Asn         G1n           Lys         Ser         Ser         Gln         Ser         Fig         Fig         Fig         Fig         Fig         G1n         Fig         Fig </td <td>Asn Asn</td> <td></td> <td></td> <td></td> <td></td> <td>62 Arg Lys</td> <td></td>	Asn Asn					62 Arg Lys	
24       25       26       27       0       b       c       d       e       d       e       d       e       d       e       d       e       d       e       d       e       d       e       d       e       d       e       d       e       d       e       d       e       d       e       d       e       d       e       d       e       d       e       d       e       d       e       d       e       e       d       e       e       d       e       d       e       e       d       e       e       d       e       e       d       e       e       d       e       e       e       d       e       e       e       e       e       e       e       e       e       e       e       e       e       e       e       e       e       e       e       e       e       e       e       e       e       e       e       e       e       e       e       e       e       e       e       e       e       e       e       e       e       e       e       e       e       e       e <td><math>\frac{30}{\text{Lys}}</math></td> <td></td> <td></td> <td></td> <td></td> <td>61 Glu <i>Gl</i>n</td> <td></td>	$\frac{30}{\text{Lys}}$					61 Glu <i>Gl</i> n	
24       25       26       27       0       b       c       d       e       d       e       d       f       l       e       d       f       e       d       f       f       f       f       f       f       f       f       f       f       f       f       f       f       f       f       f       f       f       f       f       f       f       f       f       f       f       f       f       f       f       f       f       f       f       f       f       f       f       f       f       f       f       f       f       f       f       f       f       f       f       f       f       f       f       f       f       f       f       f       f       f       f       f       f       f       f       f       f       f       f       f       f       f       f       f       f       f       f       f       f       f       f       f       f       f       f       f       f       f       f       f       f       f       f       f       f       f       f       f <td>29 Gln Ser</td> <td></td> <td></td> <td></td> <td></td> <td>60 <b>Asn</b> Ser</td> <td></td>	29 Gln Ser					60 <b>Asn</b> Ser	
1	28 Asn Asn					59 Tyr Asn	
24       25       26       27       0       b       c       d         Lys       Ser       Ser       Gln       Ser       Ieu       Ieu       Tyr         50       51       52       53       54       55       56         Trp       Ala       Ser       Thr       Arg       Glu       Ser         Trp       Ala       Ser       Thr       Arg       Glu       Ser         Gln       Gln       Tyr       Tyr       Ser       Tyr       Pro       Tyr         Gln       Gln       Tyr       Tyr       Ser       Tyr       Pro       Gly       Asp       Asp         Asp       His       Ala       Ife       His       Asp       Asp       Asp       Asp         Tyr       Ife       Asn       Ala       Gly       Asn       Gly       Asn       Asp       Asp       Asp         Ser       Icu       Asn       Wet       Ala       Gly       Ser       Gly       Ser       Eu       <	Gly Ser					58 Lys Lys	102 Tyr Tyr
Lys Ser Ser Gln Ser Leu Leu Lys Ser Ser Gln Ser Gln Ser Leu Leu Lys Ser Ser Gln Ser Val Leu Lys Ser Ser Gln Ser Val Leu Lys Ser Trp Ala Ser Thr Arg Glu Ser Trp Ala Ser Thr Arg Glu Ser Gln Gln Tyr Tyr Ser Thr Pro Gln Gln Tyr Tyr Ser Thr Pro Gln Gln His Ala IIe His Ser Tyr Ala Het His Ser Tyr Ala Gly Asn Gly Asn Gly Gly Gly Gly Asn Gly Gly Gly Tyr Tyr Cly Ser Gly Gly Gly Gly Gly Tyr Tyr Cly Ser Gly Gly Gly Gly Gly Gly Tyr Tyr Cly Ser Gly	Ser Ser		97 Thr Ser			57 Phe Thr	101  Asn
1,	Tyr.		96 Leu Tyr			Asp Asn	Ser
24 25 26 27 0 Lys Ser Ser Gln Ser Lys Ser Ser Gln Ser Lys Ser Ser Gln Ser Trp Ala Ser Thr Arg Trp Ala Ser Thr Arg Gln Gln Tyr Tyr Ser Gln Gln Tyr Tyr Ser Gln Gln Tyr Tyr Ser Tyr Ala His Ser Tyr Ala His Ser Tyr Ala His Ser Tyr Ala Gly Trp Hie Ser Pro Gly Trp Hie Asn Ala Gly Gly Cly Tyr Tyr Cly	د الم	56 Ser Ser	95 Pro			Asp Gly	Gly
24 25 26 27 Lys Ser Ser Gln Lys Ser Ser Gln Lys Ser Ser Gln Lys Ser Ser Gln Ser Trp Ala Ser Thr Gln Gln Tyr Tyr Gln Gln Tyr Tyr Gln Gln Tyr Tyr Tyr Ser Tyr Ala Ret Gly Gly Tyr Tyr Tyr Gly Gly Tyr Tyr	b Leu Val	55 Glu Glu	Tyr Thr			Asn Asn	100 Ser
24 25 26 Lys Ser Ser Lys Ser Ser Lys Ser Ser Trp Ala Ser Trp Ala Ser Trp Gln Gln Tyr	Ser Ser	Arg Arg	93 Ser		35 His H1s	53 Gly Gly	99 Ala 61 y
24 25 Lys Ser Lys Ser Lys Ser Lys Ser Trp Ala Trp Ala Gln Gln Gln Gln Gln  31 32 Asp His Ser Tyr Tyr Phe Trp Ile Gly Gly Gly Gly Gly	27 Gln Gln	53 Ala Thr	92 1yr 1yr		34 Ile	Pro Ala	98 Vet
Lys Lys Lys Ser Ser Glin Glin Glin Glin Glin Glin Glin Glin	26 Ser	Ser Ser	91 Tyr		33 Ala Ala	Ser Asn	97 Asn Tyr
E E	25 Ser	51 Ala Ala	Glu Glu		$\frac{32}{\text{His}}$	51 Phe 11e	96 [en Cly
CDR 1 HuCC49 LEN CDR 2 HuCC49 LEN CDR 3 HuCC49 21/28'CL CDR 2 HuCC49 21/28'CL CDR 3 HuCC49 21/28'CL	24 Lys Lys	50 44 44 44	Glu Glu		Asp Ser	50 Tyr	95 Ser Gly
	CDR 1 HuCC49 LEN	CDR 2 HuCC49 LEN	CDR 3 HuCC49 LEN	Heavy chain	CDR 1 HuCC49 21/28'CL	CDR 2 HuCC49 21/28'CL	CDR 3 HuCC49 21/28'CL





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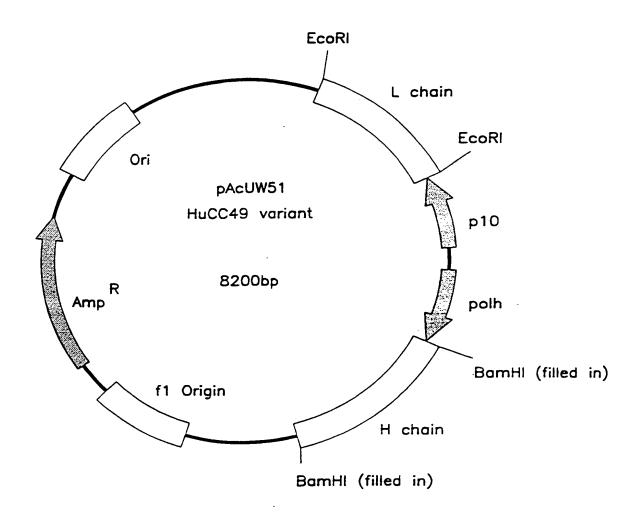
<u>FIG</u>.

Inventor: KASHMIRI et al.
Docket No.: 11613.32USWO
Title: TAIANTS OF HUMANANIZED ANTI-CARCINOMA MONOCLON
CC49
Attorne Inne: Melissa Jean Pytel
Phone No.: 612.371.5304
Sheet 5 of 23

Inventor: KASHMIRI et al.
Docket No.: 11613.32USWO

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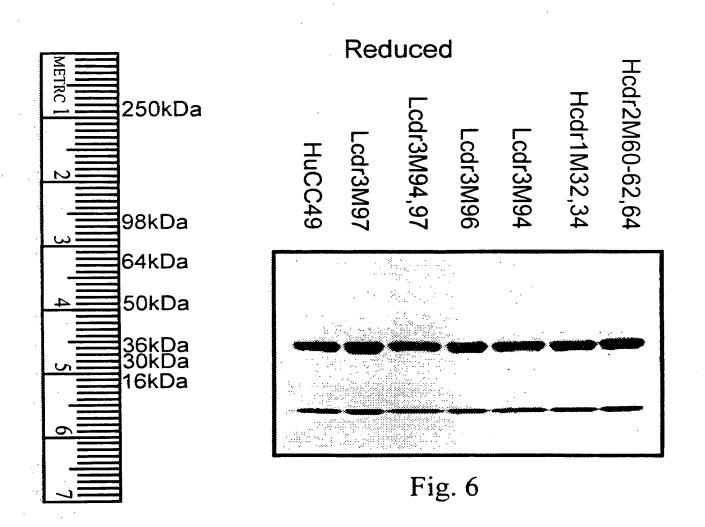
FIG. 5



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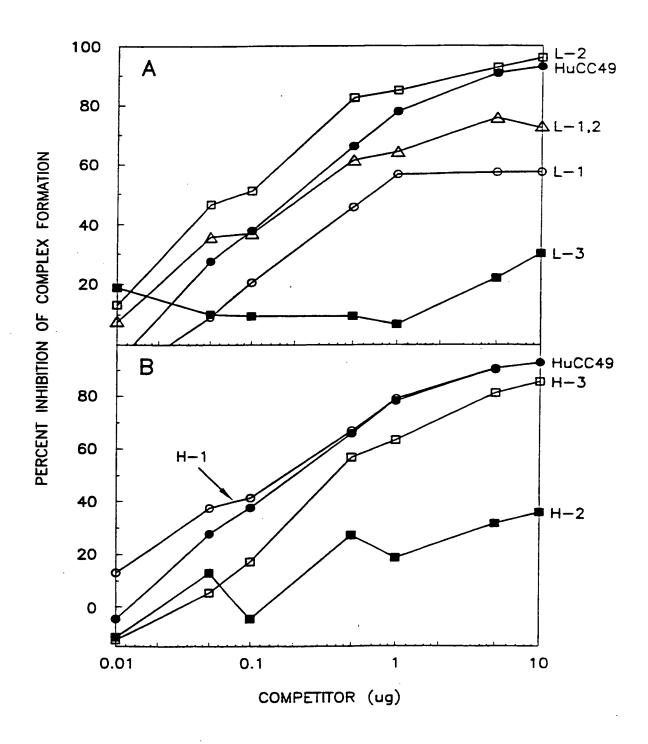
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FIG. 7



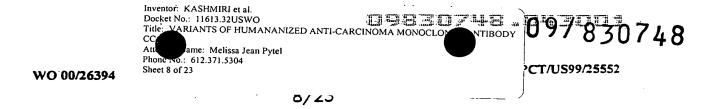
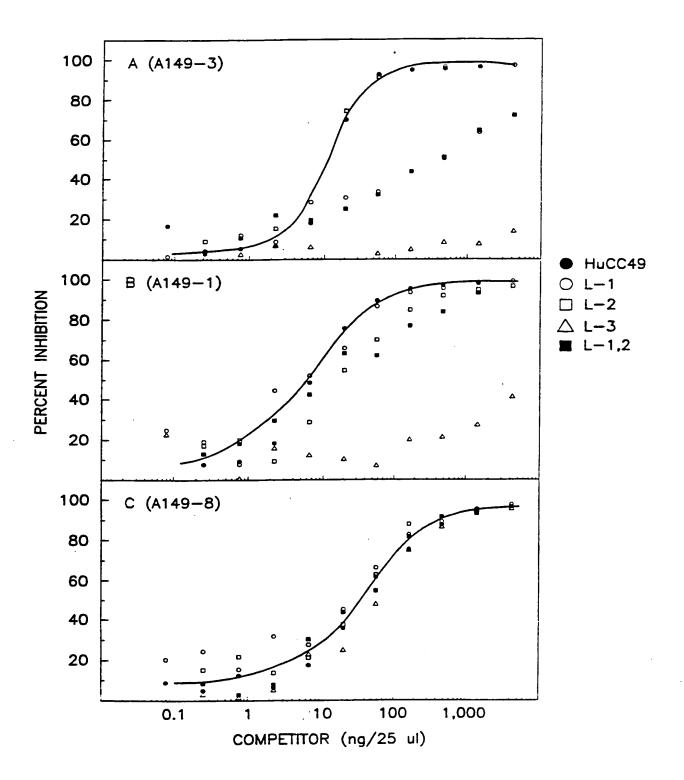


FIG. 8



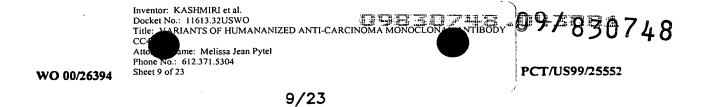


FIG. 9

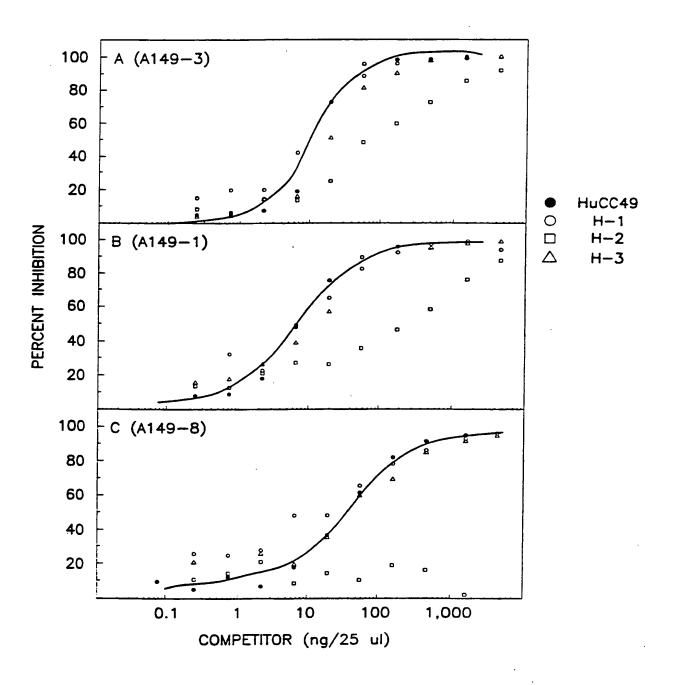
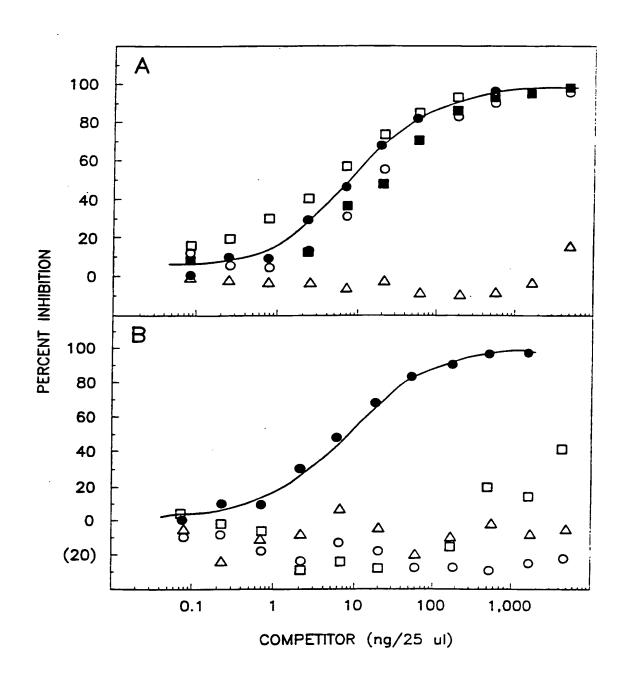


FIG. 10

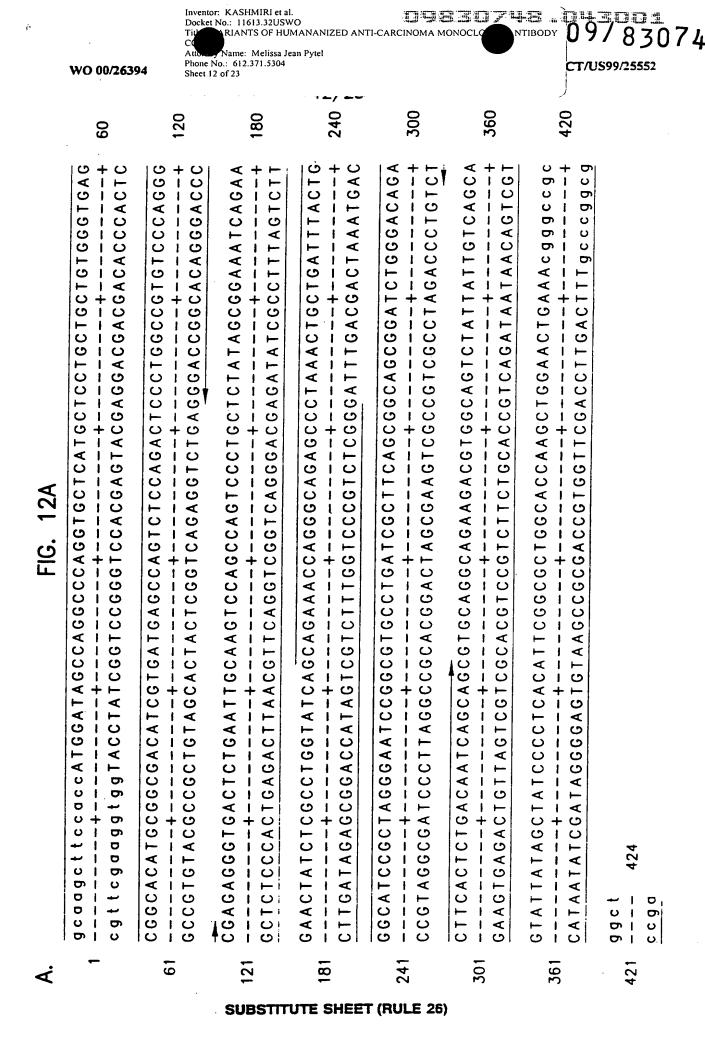


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Attorne, Name: Melissa Jean Pytel

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:	CDR1
LEN HuCC49	DIVMTQSPDSLAVSLGERATINC DIVMSQSPDSLAVSLGERVTLNC KSSQSLLYSGNQKNYLA WYQQKPGQSPKLLIY
	CDR2
LEN Hucc49	GVPDRFSGSGSGTDFTLTISSLQAEDVAVYYC WASARES GVPDRFSGSGSGTDFTLTISSVQAEDVAVYYC QQYYSYPLT FGAGTKLELK
B.	CDR1
21/28'CL QVQI HuCC49 QVQI	QVQLVQSGAEVKKPGASVKVSCKASGYTFT QVQLVQSGAEVVKPGASVKISCKASGYTFT DHAIH WVKQNPGQRLEWIG
	CDR2
21/28'CL HuCC49	RVTITRDTSASTAYMELSSLRSEDIAVYYCAR YFSPGNDDFKYNERFKG KATLTADTSASTAYVELSSLRSEDTAVYFCTR
	CDR3 · · · · ·
21/28'CL HuCC49	WGQGTLVTVSS SLNMAY WGQGTLVTVSS



Attorney Name: Melissa Jean Pytel PCT/US99/25552 Phone No.: 612.371.5304 WO 00/26394 Sheet 13 of 23 240 300 420 360 120 180 9 S ပ ပ Š S ق ပ ပ 1 ł O 1 ď ⋖ ı ပ GTCTGTGTAGACGG g ග ပ S ⋖ ပ ပ ပ i ⋖ ပ ပ ⋖ ⋖ C Q ⋖ S G ١ ⋖ g ပ O <u>ပ်</u> S S 1 9 S S S ⋖ 1 ပ ပ ပ ပ S ⋖ ⋖ -⋖ × ⋖ ⋖ ර ⋖ ⋖ ⋖ TCCGAGGATACTGCAGTGTAC ပ ı ပ 9 S ပ 1 22999 ı ⋖ ⋖ S C S 1 ပ 9 -ى ⋖ ပ ပ AGCG ⋖ ⋖ ပ ပ TCAC, ပ ර ပ ပ Ì S S ပ 1 ပ 1 ı S C ⋖ ပ ပ S 1 ⋖ 1 ⋖ 90 ර AT ပ ර S ပ ⋖ ⋖ Ġ S S ı ပ ł S ⋖ ပ ර ပ ပ ⋖ ı 1 S 1 AGA ပ AGG ပ ⋖ 1 G CGGTGTGACTGAC 1 AC ×  $\vdash$ ပ ပ ပ ပ S 1 ł ပ TCCT ت ď ပ ပ 1 1 ⋖ A G G A A AT ပ ပ 1 Þ ŀ ර S 100 A G C ပ + + 4  $\circ$ ⋖ ပ ⋖ GA S S < ပ ပ ł ⋖ 1 ပ ပ . S S CCT CCIC ပ ပ ı ⋖ ı ပ ပ 1 A C ပ ပ 1 ပ ⋖ ⋖ TAAC CAGAAGG ပ ⋖ ı ပ ⋖ 1 Q A ပ်ပ္သ ပ် Cပ G S ı ı ပ S ပ 1 ⋖ Ø Ö ت S ⋖ ı TIC GAGA ပ ı ပ ပ ပ ර 1 ပ ပ 1 ı ပ ပ  $\vdash$ GIC CTGGACAGCGCCTGGAGTG ⋖ ပ ⋖ C ⋖ -ပ ⋖ CI ⋖ ⋖ ı S ŀ ı ပ S ပ ပ ⋖ 1 S 1 S ı Ç AC C 999 ග ပ GTGCA ပ ပ  $C_{1}$ S 1 4 ပ S ပ ပ ပ ပ 1 ł ပ ပ G ပ ပ ပ ပ ပ ပ ပ 1 ı S S ı ⋖ ⋖ ပ ပ C ပ ı C ပ ပ် 4 C ⋖ 1 ⋖ ⋖ ⋖ ပ ပ ပ G ပ ර ပ ပ ပ 1 ı 1 CAC ပ G CAGCT ပ ပ 1 ပ Þ ပ 1 ⋖ A G G 9 C + × C ပ ⋖ ⋖ ပ ပ G S S S 1 i -ت Ö ⋖ ပ ပ ⋖ S ပ S ပ ပ ⋖ ı ⋖ 1 ပ ပ 1 Ğ **C** ပ ပ ပ 1 G ပ ပ ပ ပ ပ C A ⋖ ပ 1 ပ ပ ⋖ -1 ⋖ į J 6 ර ⋖ ပ ပ S GTTAC ⋖ ł ⋖ ပ  $\vdash$ 1 PG <u>ن</u> ပ ပ 9 AT 99 1 ⋖ ပ ⋖ 0 ပ ပ ⋖ Q ı ⋖ g į CA F ပ G Ø CAGAATC ပ O t ပ ⋖ ပ ပ 9 ပ δ S ⋖ ⋖ ပ ပ ပ ပ D Ö δ ⋖ ⋖ ⋖ 1 CGGAT ပ O ⋖ ⋖ Ø ပ O ပ ပ ပ ပ C S ပ ပ ပ S δ ပ 5 ⋖ ⋖ ⋖ 9 Ö ق D ပ ပ ⋖ S ⋖ ပ Ø O S ⋖ ⋖ × 4 S ပ ပ O O ⋖ ⋖ ⋖ ⋖ ပ S ပ ပ ı ı ပ δ ပ O 1 10 ⋖ ⋖ i ⋖ ı O < ł ı -1 241 121 181 301 421 6 36  $\mathbf{\omega}$ SUBSTITUTE SHEET (RULE 26)

NTS OF HUMANANIZED ANTI-CARCINOMA MONOCLONA

BODY

Inventor: KASHMIRI et al.

Docket No.: 11613.32USWO

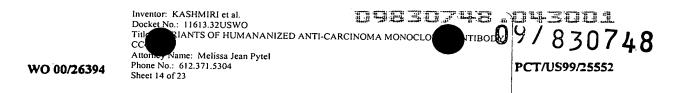
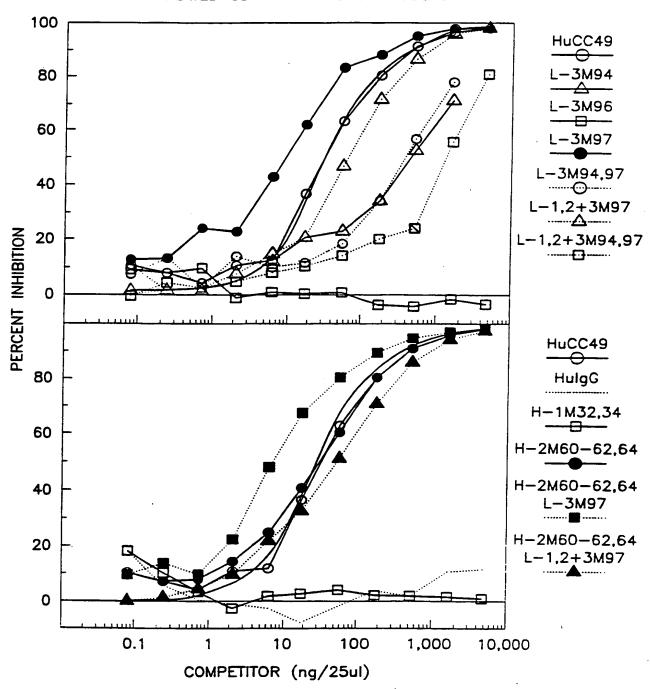


FIG. 13

## COMPETITION RADIOIMMUNASSAY: MANIPULATED CDR VARIANTS OF Hucc49



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FIG. 14

## HPLC ANALYSIS OF PATIENT REACTIVITY TO CDR SUBSTITUTION VARIANTS OF HuCC49

C	OMPETITOR		PATIENTS				
	CDR SUBSTITUTIONS	ANTIGEN BINDING	DG	СР	ΕA	DS	
NONE			46.2 <sup>b</sup>	32.2	56.8	33.5	
HuCC49		+++	0	1.5	0.5	0	
HulgG		_	59.0	N.D.	63.6	46.4	
LIGHT	L3M94	+/-	30.2	20.3	16.4	28.9	
	<b>L</b> 3М96	-	39.2	31.1	42.9	35.2	
	L3M97	+++	0.6	1.3	0.7	2.4	
	L3M94,97	+/-	26.5	18.2	18.6	25.6	
	L1,2+3M97	++	21.3	17.6	23.8	17.1	
	L1,2+3M94,97	+	53.2	38.1	44.2	37.3	
HEAVY	1M32,34	· _	1.4	5.5	3.8	0.7	
	2M60-62,64	++	24.4	17.9	21.8	16.5	
вотн	L3M97 H2M60-62,64	++++	13.0	16.1	3.9	20.1	
	L1,2+3M97 H2M60-62,64	++	33.0	30.7	24.9	32.1	

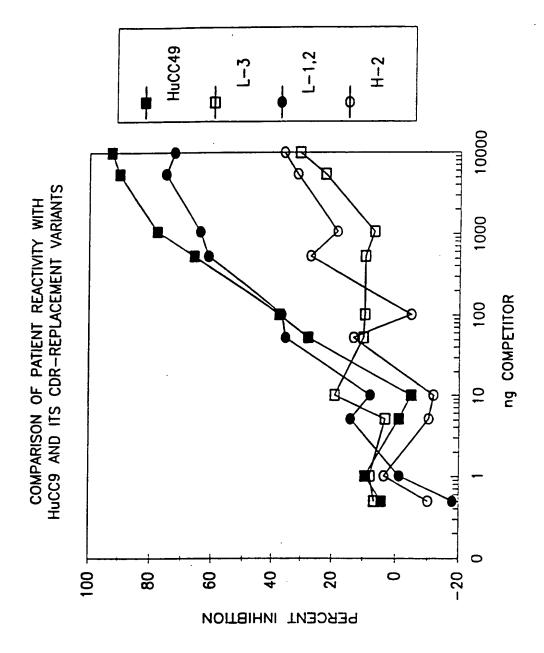
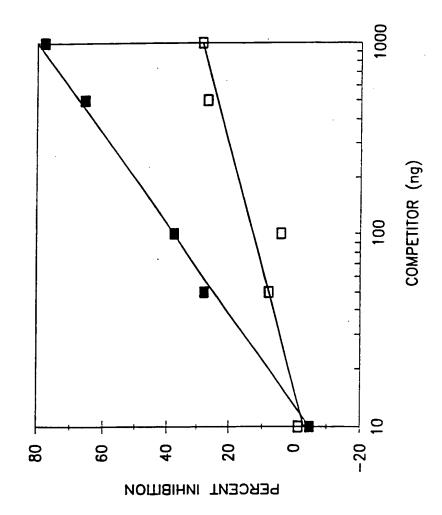


FIG. 1

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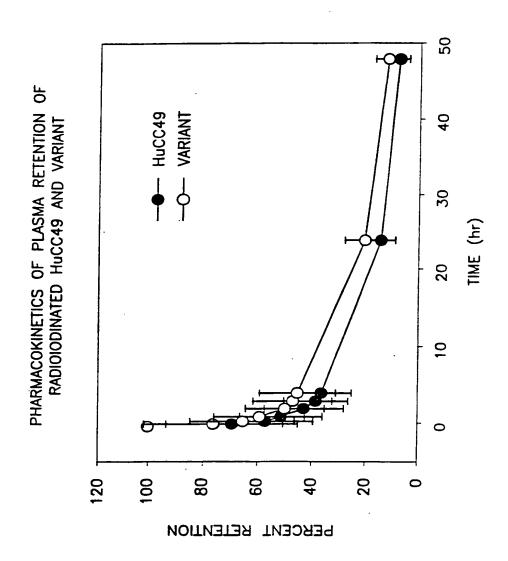
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BODY

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FIG. 18

BIODISTRIDUTION OF I.V. ADMINISTERED RADIOLABELED HUCC49 AND VARIANT IN ATHYMIC MICE BEARING LS-174T HUMAN COLON CARCINOMA XENOGRAFTS: PERCENT OF INJECTED DOSE/GRAM

			TIMEPOINTS (hr)					
ANTIBODY	ORGAN	24	48	72	120	168		
VARIANT	TUMOR	15.83	23.75	21.01	17.74	9.21		
	BLOOD	6.35	4.93	4.88	2.19	0.63		
	LIVER	3.39	2.14	1.46	0.91	0.32		
	SPLEEN	5.90	6.04	2.55	2.43	3.96		
	KIDNEY	2.52	1.27	1.00	0.77	0.36		
	LUNG	3.22	2.57	2.50	1.12	0.36		
HuCC49	TUMOR	11.86	17.59	15.31	13.75	5.24		
	BLOOD	4.17	2.94	2.85	1.29	0.18		
	LIVER	4.77	3.05	1.41	0.70	0.12		
	SPLEEN	6.41	7.47	2.28	2.00	0.46		
	KIDNEY	1.86	0.92	0.70	0.57	0.14		
	LUNG	2.17	1.58	1.46	0.68	0.12		

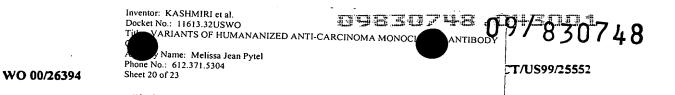
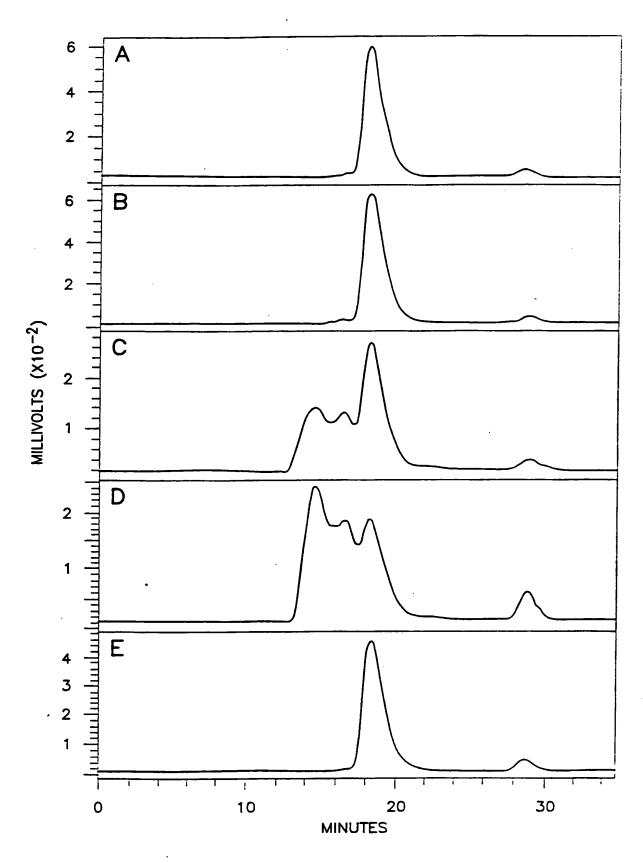


FIG. 19



**SUBSTITUTE SHEET (RULE 26)** 

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FIG. 20

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